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# Identification of p2y9/GPR23 as a novel G protein-coupled receptor for Lysophosphatidic acid, structurally distant from the Edg family

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Lysophosphatidic acid (LPA) is a bioactive lipid mediator with diverse physiological and pathological actions on many types of cells. LPA has been widely considered to elicit its biological functions through three types of G protein-coupled receptors, Edg (endothelial cell differentiation gene) 2/LPA1/Vzg (ventricular zone gene) 1, Edg4/LPA2 and Edg7/LPA3. We identified an orphan G protein-coupled receptor, p2y9/GPR23, as the fourth LPA receptor (LPA4). Membrane fractions of RH7777 cells transiently expressing p2y9/GPR23 displayed a specific binding for 1-oleoyl-LPA with a K<sub>d</sub> value of around 45 nM. Competition binding and reporter gene assays showed that p2y9/GPR23 preferred structural analogs of LPA with a rank order of 1-oleoyl- > 1-stearoyl- > 1-palmitoyl- > 1-myristoyl- > 1-alkyl- > 1-alkenyl-LPA. In Chinese hamster ovary cells expressing p2y9/GPR23, 1-oleoyl-LPA induced an increase in [Ca<sup>2+</sup>]<sub>i</sub>, and stimulated adenylyl cyclase activity. Quantitative Real time-PCR demonstrated that mRNA of p2y9/GPR23 was significantly abundant in ovary compared to other tissues. Interestingly, p2y9/GPR23 shares only 20-24% amino acid identities with Edg2, Edg4 and Edg7, and phylogenetic analysis also shows that p2y9/GPR23 is far distant from the Edg family. These facts suggest that p2y9/GPR23 has evolved from different ancestor sequences from the Edg family.

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C. Zhao, M. J. Fernandes, G. D. Prestwich, M. Turgeon, J. Di Battista, T. Clair, P. E. Poubelle, and S. G. Bourgoin

**Regulation of Lysophosphatidic Acid Receptor Expression and Function in Human Synoviocytes: Implications for Rheumatoid Arthritis?**

Mol. Pharmacol., February 1, 2008; 73(2): 587 - 600.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

J. Chen, A. R. Baydoun, R. Xu, L. Deng, X. Liu, W. Zhu, L. Shi, X. Cong, S. Hu, and X. Chen

**Lysophosphatidic Acid Protects Mesenchymal Stem Cells Against Hypoxia and Serum Deprivation-Induced Apoptosis**

Stem Cells, January 1, 2008; 26(1): 135 - 145.

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page

F.-T. Lin, Y.-J. Lai, N. Makarova, G. Tigyi, and W.-C. Lin

**The Lysophosphatidic Acid 2 Receptor Mediates Down-regulation of Siva-1 to Promote Cell Survival**

J. Biol. Chem., December 28, 2007; 282(52): 37759 - 37769.

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page

K. Hama, J. Aoki, A. Inoue, T. Endo, T. Amano, R. Motoki, M. Kanai, X. Ye, J. Chun, N. Matsuki, *et al.*

**Embryo Spacing and Implantation Timing Are Differentially Regulated by LPA3-Mediated Lysophosphatidic Acid Signaling in Mice**

Biol Reprod, December 1, 2007; 77(6): 954 - 959.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

M. M. Murph, J. Hurst-Kennedy, V. Newton, D. N. Brindley, and H. Radhakrishna

**Lysophosphatidic Acid Decreases the Nuclear Localization and Cellular Abundance of the p53 Tumor Suppressor in A549 Lung Carcinoma Cells**

Mol. Cancer Res., November 1, 2007; 5(11): 1201 - 1211.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

K. M. Kassel, N. A. Schulte, S. M. Parker, A. D. Lanik, and M. L. Toews

**Lysophosphatidic Acid Decreases Epidermal Growth Factor Receptor Binding in Airway Epithelial Cells**

J. Pharmacol. Exp. Ther., October 1, 2007; 323(1): 109 - 118.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

Y.-J. Lai, W.-C. Lin, and F.-T. Lin

**PTPL1/FAP-1 Negatively Regulates TRIP6 Function in Lysophosphatidic Acid-induced Cell Migration**

J. Biol. Chem., August 17, 2007; 282(33): 24381 - 24387.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

C. E. Horak, J. H. Lee, A. G. Elkahloun, M. Boissan, S. Dumont, T. K. Maga, S. Arnaud-Dabernat, D. Palmieri, W. G. Stetler-Stevenson, M.-L. Lacombe, *et al.*

**Nm23-H1 Suppresses Tumor Cell Motility by Down-regulating the Lysophosphatidic Acid Receptor EDG2**

Cancer Res., August 1, 2007; 67(15): 7238 - 7246.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

Y. Zhao, D. He, J. Zhao, L. Wang, A. R. Leff, E. Wm. Spannhake, S. Georas, and V. Natarajan

**Lysophosphatidic Acid Induces Interleukin-13 (IL-13) Receptor {alpha}2 Expression and Inhibits IL-13 Signaling in Primary Human Bronchial Epithelial Cells**

J. Biol. Chem., April 6, 2007; 282(14): 10172 - 10179.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

K. Yanagida, S. Ishii, F. Hamano, K. Noguchi, and T. Shimizu

**LPA4/p2y9/GPR23 Mediates Rho-dependent Morphological Changes in a Rat Neuronal Cell Line**

J. Biol. Chem., February 23, 2007; 282(8): 5814 - 5824.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

C.-W. Lee, R. Rivera, A. E. Dubin, and J. Chun

**LPA4/GPR23 Is a Lysophosphatidic Acid (LPA) Receptor Utilizing Gs-, Gq/Gi-mediated Calcium Signaling and G12/13-mediated Rho Activation**

J. Biol. Chem., February 16, 2007; 282(7): 4310 - 4317.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

S. Choi, M. Lee, A. L. Shiu, S. J. Yo, and G. W. Aponte

**Identification of a protein hydrolysate responsive G protein-coupled receptor in enterocytes**

Am J Physiol Gastrointest Liver Physiol, January 1, 2007; 292(1): G98 - G112.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

☒ Home  
page

D.-J. Jun, J.-H. Lee, B.-H. Choi, T.-K. Koh, D.-C. Ha, M.-W. Jeong, and K.-T. Kim

**Sphingosine-1-Phosphate Modulates Both Lipolysis and Leptin Production in Differentiated Rat White Adipocytes**

Endocrinology, December 1, 2006; 147(12): 5835 - 5844.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

S. Rieken, S. Herroeder, A. Sassmann, B. Wallenwein, A. Moers, S. Offermanns, and N. Wettschureck

**Lysophospholipids Control Integrin-dependent Adhesion in Splenic B Cells through Gi and G12/G13 Family G-proteins but Not through Gq/G11**

J. Biol. Chem., December 1, 2006; 281(48): 36985 - 36992.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

M. Murph, T. Tanaka, S. Liu, and G. B. Mills

**Of Spiders and Crabs: The Emergence of Lysophospholipids and Their Metabolic Pathways as Targets for Therapy in Cancer.**

Clin. Cancer Res., November 15, 2006; 12(22): 6598 - 6602.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

Z. Zhang, Z. Liu, and K. E. Meier

**Lysophosphatidic acid as a mediator for proinflammatory agonists in a human corneal epithelial cell line**

Am J Physiol Cell Physiol, November 1, 2006; 291(5): C1089 - C1098.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

R. Guo, E. A. Kasbohm, P. Arora, C. J. Sample, B. Baban, N. Sud, P. Sivashanmugam, N. H. Moniri, and Y. Daaka

**Expression and Function of Lysophosphatidic Acid LPA1 Receptor in Prostate Cancer Cells**

Endocrinology, October 1, 2006; 147(10): 4883 - 4892.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

M. P. Abbracchio, G. Burnstock, J.-M. Boeynaems, E. A. Barnard, J. L. Boyer, C. Kennedy, G. E. Knight, M. Fumagalli, C. Gachet, K. A. Jacobson, *et al.*

**International Union of Pharmacology LVIII: Update on the P2Y G Protein-Coupled Nucleotide Receptors: From Molecular**

## Mechanisms and Pathophysiology to Therapy

Pharmacol. Rev., September 1, 2006; 58(3): 281 - 341.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

M. Tanaka, S. Okudaira, Y. Kishi, R. Ohkawa, S. Iseki, M. Ota, S. Noji, Y. Yatomi, J. Aoki, and H. Arai

### **Autotaxin Stabilizes Blood Vessels and Is Required for Embryonic Vasculature by Producing Lysophosphatidic Acid**

J. Biol. Chem., September 1, 2006; 281(35): 25822 - 25830.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

C.-W. Lee, R. Rivera, S. Gardell, A. E. Dubin, and J. Chun

### **GPR92 as a New G12/13- and Gq-coupled Lysophosphatidic Acid Receptor That Increases cAMP, LPA5**

J. Biol. Chem., August 18, 2006; 281(33): 23589 - 23597.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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D. L. Baker, Y. Fujiwara, K. R. Pigg, R. Tsukahara, S. Kobayashi, H. Murofushi, A. Uchiyama, K. Murakami-Murofushi, E. Koh, R. W. Bandle, et al.

### **Carba Analogs of Cyclic Phosphatidic Acid Are Selective Inhibitors of Autotaxin and Cancer Cell Invasion and Metastasis**

J. Biol. Chem., August 11, 2006; 281(32): 22786 - 22793.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

K. Kotarsky, A. Boketoft, J. Bristulf, N. E. Nilsson, A. Norberg, S. Hansson, C. Owman, R. Sillard, L. M. F. Leeb-Lundberg, and B. Olde  
**Lysophosphatidic Acid Binds to and Activates GPR92, a G Protein-Coupled Receptor Highly Expressed in Gastrointestinal Lymphocytes**

J. Pharmacol. Exp. Ther., August 1, 2006; 318(2): 619 - 628.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

C. L. Sayas, A. Ariaens, B. Ponsioen, and W. H. Moolenaar  
**GSK-3 Is Activated by the Tyrosine Kinase Pyk2 during LPA1-mediated Neurite Retraction**

Mol. Biol. Cell, April 1, 2006; 17(4): 1834 - 1844.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

K. S. Park, H.-Y. Lee, M.-K. Kim, E. H. Shin, S. H. Jo, S. D. Kim, D.-S. Im, and Y.-S. Bae

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	<b>Lysophosphatidylserine Stimulates L2071 Mouse Fibroblast Chemotactic Migration via a Process Involving Pertussis Toxin-Sensitive Trimeric G-Proteins</b>	
	Mol. Pharmacol., March 1, 2006; 69(3): 1066 - 1073.	
	<a href="#">[Abstract]</a> <a href="#">[Full Text]</a> <a href="#">[PDF]</a>	

<input checked="" type="checkbox"/> Home page		
	<b>T. Tsukahara, R. Tsukahara, S. Yasuda, N. Makarova, W. J. Valentine, P. Allison, H. Yuan, D. L. Baker, Z. Li, R. Bittman, <i>et al.</i></b>	
	<b>Different Residues Mediate Recognition of 1-O-Oleyllysophosphatidic Acid and Rosiglitazone in the Ligand Binding Domain of Peroxisome Proliferator-activated Receptor {gamma}</b>	
	J. Biol. Chem., February 10, 2006; 281(6): 3398 - 3407. <a href="#">[Abstract]</a> <a href="#">[Full Text]</a> <a href="#">[PDF]</a>	

<input checked="" type="checkbox"/> Home page		
	<b>M. Rahaman, R. W. Costello, K. E. Belmonte, S. S. Gendy, and M.-T. Walsh</b>	
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	Am. J. Respir. Cell Mol. Biol., February 1, 2006; 34(2): 233 - 241. <a href="#">[Abstract]</a> <a href="#">[Full Text]</a> <a href="#">[PDF]</a>	

<input checked="" type="checkbox"/> Home page		
	<b>J. Rubenfeld, J. Guo, N. Sookrung, R. Chen, W. Chaicumpa, V. Casolaro, Y. Zhao, V. Natarajan, and S. Georas</b>	
	<b>Lysophosphatidic acid enhances interleukin-13 gene expression and promoter activity in T cells</b>	
	Am J Physiol Lung Cell Mol Physiol, January 1, 2006; 290(1): L66 - L74. <a href="#">[Abstract]</a> <a href="#">[Full Text]</a> <a href="#">[PDF]</a>	

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	<b>N. M. Urs, K. T. Jones, P. D. Salo, J. E. Severin, J. Trejo, and H. Radhakrishna</b>	
	<b>A requirement for membrane cholesterol in the {beta}-arrestin- and clathrin-dependent endocytosis of LPA1 lysophosphatidic acid receptors</b>	
	J. Cell Sci., November 15, 2005; 118(22): 5291 - 5304. <a href="#">[Abstract]</a> <a href="#">[Full Text]</a> <a href="#">[PDF]</a>	

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	<b>D. A. Lin and J. A. Boyce</b>	
	<b>IL-4 Regulates MEK Expression Required for Lysophosphatidic Acid-Mediated Chemokine Generation by Human Mast Cells</b>	
	J. Immunol., October 15, 2005; 175(8): 5430 - 5438. <a href="#">[Abstract]</a> <a href="#">[Full Text]</a> <a href="#">[PDF]</a>	

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A. A. Maghazachi

**Insights into Seven and Single Transmembrane-Spanning Domain Receptors and Their Signaling Pathways in Human Natural Killer Cells**

Pharmacol. Rev., September 1, 2005; 57(3): 339 - 357.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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W. T. Wu, C.-N. Chen, C. I. Lin, J. H. Chen, and H. Lee

**Lysophospholipids Enhance Matrix Metalloproteinase-2 Expression in Human Endothelial Cells**

Endocrinology, August 1, 2005; 146(8): 3387 - 3400.

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M. Yang, W. W. Zhong, N. Srivastava, A. Slavin, J. Yang, T. Hoey, and S. An

**G protein-coupled lysophosphatidic acid receptors stimulate proliferation of colon cancer cells through the {beta}-catenin pathway**

PNAS, April 26, 2005; 102(17): 6027 - 6032.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

S. Ishii, Y. Kihara, and T. Shimizu

**Identification of T Cell Death-associated Gene 8 (TDAG8) as a Novel Acid Sensing G-protein-coupled Receptor**

J. Biol. Chem., March 11, 2005; 280(10): 9083 - 9087.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

K. Itagaki, K. B. Kannan, and C. J. Hauser

**Lysophosphatidic acid triggers calcium entry through a non-store-operated pathway in human neutrophils**

J. Leukoc. Biol., February 1, 2005; 77(2): 181 - 189.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

S. Bagga, K. S. Price, D. A. Lin, D. S. Friend, K. F. Austen, and J. A. Boyce

**Lysophosphatidic acid accelerates the development of human mast cells**

Blood, December 15, 2004; 104(13): 4080 - 4087.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)



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page

N. Murakami, T. Yokomizo, T. Okuno, and T. Shimizu

**G2A Is a Proton-sensing G-protein-coupled Receptor Antagonized by Lysophosphatidylcholine**

J. Biol. Chem., October 8, 2004; 279(41): 42484 - 42491.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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R. Cummings, Y. Zhao, D. Jacoby, E. W. Spannhake, M. Ohba, J. G. N. Garcia, T. Watkins, D. He, B. Saatian, and V. Natarajan

**Protein Kinase C $\delta$  Mediates Lysophosphatidic Acid-induced NF- $\kappa$ B Activation and Interleukin-8 Secretion in Human Bronchial Epithelial Cells**

J. Biol. Chem., September 24, 2004; 279(39): 41085 - 41094.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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B. Anliker and J. Chun

**Lysophospholipid G Protein-coupled Receptors**

J. Biol. Chem., May 14, 2004; 279(20): 20555 - 20558.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

K. Hama, J. Aoki, M. Fukaya, Y. Kishi, T. Sakai, R. Suzuki, H. Ohta, T. Yamori, M. Watanabe, J. Chun, *et al.*

**Lysophosphatidic Acid and Autotaxin Stimulate Cell Motility of Neoplastic and Non-neoplastic Cells through LPA1**

J. Biol. Chem., April 23, 2004; 279(17): 17634 - 17639.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

C. Zhang, D. L. Baker, S. Yasuda, N. Makarova, L. Balazs, L. R. Johnson, G. K. Marathe, T. M. McIntyre, Y. Xu, G. D. Prestwich, *et al.*

**Lysophosphatidic Acid Induces Neointima Formation Through PPAR $\gamma$  Activation**

J. Exp. Med., March 15, 2004; 199(6): 763 - 774.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

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page

J. Xu, Y.-J. Lai, W.-C. Lin, and F.-T. Lin

**TRIP6 Enhances Lysophosphatidic Acid-induced Cell Migration by Interacting with the Lysophosphatidic Acid 2 Receptor**

J. Biol. Chem., March 12, 2004; 279(11): 10459 - 10468.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

<input type="checkbox"/> Home page	<p>D.-S. Im  <b>Discovery of new G protein-coupled receptors for lipid mediators</b>          J. Lipid Res., March 1, 2004; 45(3): 410 - 418.  <a href="#">[Abstract]</a> <a href="#">[Full Text]</a> <a href="#">[PDF]</a></p>
------------------------------------	---

<input type="checkbox"/> Home page	<p>T. Yamada, K. Sato, M. Komachi, E. Malchinkhuu, M. Tobo, T. Kimura, A. Kuwabara, Y. Yanagita, T. Ikeya, Y. Tanahashi, <i>et al.</i>  <b>Lysophosphatidic Acid (LPA) in Malignant Ascites Stimulates Motility of Human Pancreatic Cancer Cells through LPA1</b>          J. Biol. Chem., February 20, 2004; 279(8): 6595 - 6605.  <a href="#">[Abstract]</a> <a href="#">[Full Text]</a> <a href="#">[PDF]</a></p>
------------------------------------	--

<input type="checkbox"/> Home page	<p>H. Ohta, K. Sato, N. Murata, A. Damirin, E. Malchinkhuu, J. Kon, T. Kimura, M. Tobo, Y. Yamazaki, T. Watanabe, <i>et al.</i>  <b>Ki16425, a Subtype-Selective Antagonist for EDG-Family Lysophosphatidic Acid Receptors</b>          Mol. Pharmacol., October 1, 2003; 64(4): 994 - 1005.  <a href="#">[Abstract]</a> <a href="#">[Full Text]</a> <a href="#">[PDF]</a></p>
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